

II. Amendments to the Specification

Kindly amend the specification as follows:

Page 1, line 2, please strike the paragraph and replace it with the following replacement paragraph:

--CROSS-REFERENCE TO RELATED APPLICATIONS

*B*¹ This application is a continuation-in-part of U.S. patent application, serial no. 09/488,644, filed January 21, 2000, now abandoned, and a continuation of international application PCT/DK01/00036, filed January 18, 2001.--

Pages 7-8, beginning at page 7, line 21 - page 8, line 2, please delete the paragraph and insert the following replacement paragraph.

As it is further shown in the below examples, when using the HPLC-MS method the inventors observed in cells grown on a nutritional medium containing a porphyrin compound both under anaerobic and aerobic conditions clear peaks in the porphyrin region. No cytochromes were detected in cells cultured in a medium without haemin.

*B*² However, it has been found that it is possible to detect cytochromes at a relatively high level in the modified cells after they have been transferred to a medium wherein the cells are capable of replicating. This is a very surprising finding, as it has not hitherto been shown that lactic acid bacterial cells grown under aerobic conditions in the presence of a porphyrin compound ~~has~~ have an increased content of cytochromes and that the culturally modified cells contain cytochromes after inoculation into a medium wherein the cells are capable of replicating. Without intending to limit the invention in any way, the inventors propose that a bacterial cell grown under aerobic conditions may, through the action of an NADH oxidase, regenerate the required NAD⁺ under

B² oxygen consumption. If a porphyrin compound is present in the culture medium under aerobic conditions the bacterial cells produce cytochromes and, due to the cytochrome dependent respiration, oxygen is reduced to water with the formation of metabolically usable energy, such as ATP and NAD⁺.

Pages 9-10, beginning at page 9, line 34 - page 10, line 3, please delete the paragraph and insert the following replacement paragraph:

B³ Thus, in a preferred embodiment of the present invention, the culturally modified lactic acid bacterial cells are cells which, when they are inoculated at a concentration of about 10⁷ cells/ml into low pasteurised skimmed milk having 8 ppm of dissolved oxygen and leaving the milk to stand for about 2 hours at a temperature of about 30°C, ~~consumes~~ consume at least 25% of the oxygen.

Page 10, lines 4-8, please delete the paragraph and insert the following replacement paragraph.

B⁴ However, the culturally modified lactic acid bacterial cells according to the invention may be particularly useful when the cells under the above conditions ~~consumes~~ consume at least 30% of the oxygen present in the milk, including at least 40%, such as at least 50%, e.g. at least 60%, such as at least 70%, e.g. at least 80%, such as at least 90%, e.g. at least 95% of the dissolved oxygen.

Page 10, lines 10-23, please delete the paragraph and insert the following replacement paragraph.

B⁵ It has been found that a culturally modified lactic acid bacterial cell according to the invention has, relative to the cell from which it is derived, an altered NADH oxidase,

B⁵
i.e. NOX activity, and/or lactate dehydrogenase (LDH) activity. As explained above, cells grown under aerobic condition may be capable of regenerating the required energy from other systems induced during aerobic fermentation and maintained during the inoculation of the cells into milk or any other non-porphyrin-containing or low-porphyrin-containing starter material. Thus, in preferred embodiments of the present invention the culturally modified cell is a cell which, relative to the cell from which it is derived, has a decreased NOX activity and/or a decreased LDH activity. It will be understood that the NOX enzyme, which is encoded by the *nox* gene, is one example of an H₂O forming NADH oxidase. This enzyme regenerates two equivalents of NAD⁺ under consumption of molecular oxygen. Further examples of NADH oxidases which could be present in a cell according to the invention are non-haeme flavoproteins where two types have been reported, one of which catalyses the reduction of O₂ to H₂O₂, the other one the reduction of O₂ to H₂O.

Page 14, lines 24-30, please delete the paragraph and insert the following replacement paragraph.

B⁶
Yet another significant embodiment of the method according to the present invention is where the culturally modified bacterial cells ~~is~~ are derived from a bacterial culture generally referred to as a probiotic culture. By the term "probiotic" is in the present context understood a microbial culture which, when ingested in the form of viable cells by humans or animals, confers an improved health condition, e.g. by suppressing harmful microorganisms in the gastrointestinal tract, by enhancing the immune system or by contributing to the digestion of nutrients.

Page 15, lines 13 -21, please delete the paragraph and insert the following replacement paragraph.

B⁷ It is also an objective of the present invention to provide a method of preparing a fermented food or feed product based on the use of the culturally modified lactic acid bacterial strain according to the invention. In its broadest aspect, such method comprises that an effective amount of the culturally modified lactic acid bacterial cells according to the invention or a composition comprising the modified cells are added to a food or feed product starting material, wherein the cells or the composition ~~is~~ are capable of fermenting said starting material to obtain the fermented food or feed. It will be appreciated that in such a method one or more strains of non-metabolically modified lactic acid bacteria can be used in addition to the modified lactic acid bacteria.

Pages 15-16, starting at page 15, line 31 - page 16, line 5, please delete the paragraph and insert the following replacement paragraph.

B⁸ It is yet another objective of the invention to provide the use of the culturally modified lactic acid bacterial cells of the invention or the composition comprising such cells for the production of a metabolite produced by the cell or the composition. In the present context "produced by the cell or the composition" implies that the metabolite can be one that is naturally produced by the cells or that the metabolite is produced recombinantly by the modified cells. In an alternative embodiment, the production of the metabolite is achieved by co-cultivating a modified cell of the invention with at least one non-modified organism capable of producing the metabolite. Typical examples of metabolites that ~~is~~ are produced by the cells include lactic acid, acetaldehyde, α -acetolactate, acetoin, acetate, ethanol, diacetyl and 2,3-butylene glycol.

Page 16, lines 12-13, please delete the paragraph and insert the following replacement paragraph.

B⁹ The invention will now be described in further details in the following non-limiting examples and the drawings, wherein

Page 16, line 14, please insert the following heading.

BRIEF DESCRIPTION OF THE DRAWINGS